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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,860	06/30/2006	Ariel G. Notcovich	27396U	3336

20529 7590 01/06/2011

THE NATH LAW GROUP
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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
01/06/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,860	NOTCOVICH ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-37,39 and 41-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-37, 39, 41-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/15/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 29 and 37 are objected to because of the following informalities.

In claim 29, line 3, "member" should be --members--, since there needs to be more than one member for there to be simultaneous adsorbing. Likewise with line14, “member" should be --members--.

For the same reason, in claim 37, lines 8 and 12, respectively, “member” should be –members--.

Appropriate correction is required.

Applicant has argued that “simultaneous” in the claims can encompass the first and second binding members simultaneously provided. However, Examiner does not see any support for this interpretation in the specification. To the contrary, all the disclosed embodiments provide the first binding member and second binding member sequentially with each other, and there is no support as to how the first and second binding members are provided or absorbed at the same time.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 29-31, 33, 35-37, 41, 42 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler et al., 5,384,261, in view of Ivarsson, 6,493,097, and further in view of Shah, 6,916,621.

Winkler et al. teach the synthesis of an array of different peptides in selected regions of a substrate. Such substrates having the diverse sequences formed thereon may be used in, for example, screening studies to evaluate their interaction with receptors such as antibodies. For example, in preferred embodiments the invention provides for screening of peptides to determine which if any of a diverse set of peptides has strong binding affinity with a receptor and, in most preferred embodiments to determine the relative binding affinity of various peptides with a receptor of interest such as an antibody. Column 6, lines 6-20.

In operation, the substrate may be provided with appropriate linker molecules on the surface thereof. Thereafter, the surface is provided with protected surface active groups. Column 9, lines 15-28.

Thereafter, the channel block and the substrate are brought into contact forming fluid-tight channels bounded by the grooves in the channel block and the substrate. When the channel block and the substrate are in contact, a protective group removal agent is, thereafter, directed through a first selected channel or group of channels by placing the pipettor on the flow inlet of the selected channel and, optionally, the vacuum source on the outlet of the channel. In the case of, for example, TBOC protected amino acids, this protective group removal agent may be, for example,

trifluoroacetic acid (TFA). This step is optionally followed by steps of washing to remove excess TFA with, for example, dichloromethane (DCM). Column 9, lines 29-42.

Thereafter, a first amino acid or other monomer A is directed through the first selected flow channel. Preferably this first amino acid is also provided with an appropriate protective group such as TBOC, FMOC, nitroveratryloxycarbonyl (NVOC) or the like. This step is also followed by appropriate washing steps. These steps of deprotection/coupling are concurrently with or thereafter repeated for additional channels parallel to the first channel(s) which are to be provided with the same or different monomers. Column 9, lines 43-52.

Thereafter, the substrate and the channel block are separated and, optionally, the entire substrate is washed with an appropriate material to remove any unwanted materials from the points where the channels contact the substrate. Column 9, lines 53-57.

The substrate and/or block is then, optionally, washed and translated and/or rotated with the stage. In preferred embodiments, the substrate is rotated 90 degrees from its original position, although some embodiments may provide for greater or less rotation, such as from 0 to 180 degrees. Column 9, line 58 – column 10, line 3.

The steps of deprotection, and coupling of amino acids or other monomers is then repeated, resulting in the formation of an array of polymers on the surface of the substrate. For example, a monomer B may be directed through selected flow channels, providing the polymer AB at intersections of the channels formed by the channel block in the first position with the channels formed by the

channel block after 90-degree rotation. Column 10, lines 4-11. Examiner emphasizes here that these steps are part of the method of synthsis of the array.

According to preferred embodiments, the array of polymer sequences is utilized in one or more of a variety of screening processes. For example, the substrate is then exposed to a receptor of interest such as an enzyme or antibody. According to preferred embodiments, the receptor is labelled with fluorescein, or otherwise labelled, so as to provide for easy detection of the location at which the receptor binds. According to some embodiments, the channel block is used to direct solutions containing a receptor over a synthesized array of polymers. For example, according to some embodiments the channel block is used to direct receptor solutions having different receptor concentrations over regions of the substrate.

Col 11, line 17-35.

It is also disclosed that diverse polymer sequences are preferably synthesized on a single substrate. By synthesizing the diverse polymer sequences on a single substrate, processing of the sequences to evaluate their characteristics, such as relative binding affinity, is more easily conducted. By way of example, when a variety of peptide sequences are to be evaluated to determine their relative binding affinity to a receptor, the entire substrate and, therefore, all or a group of the polymer sequences may be exposed to an appropriately labelled receptor and evaluated simultaneously. Column 6, lines 21-31.

The invention allows for coupling of additional monomer in a polymer, and that monomers may be introduced concurrently through the channels and thus only a single process step is required to perform two coupling steps simultaneously. Column 6, lines 50-66.

It is disclosed that diverse polymer sequences are preferably synthesized on a single substrate. By synthesizing the diverse polymer sequences on a single substrate, processing of the sequences to evaluate their characteristics, such as relative binding affinity, is more easily conducted. By way of example, when a variety of peptide sequences are to be evaluated to determine their relative binding affinity to a receptor, the entire substrate and, therefore, all or a group of the polymer sequences may be exposed to an appropriately labelled receptor and evaluated simultaneously. Column 6, lines 21-31.

Thus as to claims 29, 33 and 37, Winkler disclose activating (providing a deprotector) through the channels, simultaneously adsorbing first binding members through the channels, and deactivating (providing another protective group) and simultaneously providing second binding members through the channels. Also disclosed is using the channel block to direct receptor solutions having different receptor concentrations over regions of the substrate [array] (col. 11, line 17-35).

Applicant also claims simultaneously obtaining one or more kinetic parameters indicative of a binding reaction between the first binding member and the second binding member at each of the plurality of microspots to produce a kinetic analysis of the binding. Kinetic measurements are not discussed by Winkler et al.

However, Ivarrson teach an improved method that allows for each sensor zone to be monitored simultaneously (column 7, line 60 – column 18, line 7.) Ivarrson also teaches that instead of measuring and presenting surface concentrations, it is possible to measure and present surface concentration changes, surface refractive indexes, surface refractive index changes, surface thicknesses and surface thickness changes. The amounts of sample species bound or adsorbed to the different sensor spots or subzones may be related to each other by analytical software. The time relation of the refractometric images makes it possible to obtain via further image data processing mass distribution kinetic data for, e.g., specific sample binding/desorption, sample displacement along the sensor surface, or for the separation process. Column 23, lines 53-64.

It is also disclosed by Ivarrson that types of optical principles used may be for example surface plasmon resonance (SPR), Brewster angle (both internal and external), ellipsometry angle (both internal and external), critical angle, and frustrated total reflection waveguide resonance. Column 9, lines 40-48.

Applicant also claims that the plurality of bindings carried out do not necessitate a regeneration step. It is disclosed in Applicant's specification in paragraph 0006 that as is known in the art and in commercially available devices, a standard kinetic binding interaction measurement includes washing and regeneration of the probe. That is, the second binding member (target) is removed so that another concentration of the target is contacted with the probe.

This is disclosed by Winkler in detecting that the different channels may be provided with different concentrations of analyte [[receptor"] channels, and detected simultaneously (column 11, lines 17-35.)

Using the Winkler device as discussed above does not necessitate a regeneration step in order to provide the different concentrations of analyte since they are provided through the different channels and detected simultaneously, as this is understood to be the case for the analyte as it is for the process of immobilizing the first binding reagent. The skilled artisan would have had reasonable expectation of success in performing kinetic analysis (suggested by Ivarrson) with different concentrations of analyte in the different channels because it is predictable that the same binding detection can be made in each channel over a period of time to obtain kinetic data.

In other words, it is predictable by the skilled artisan that simultaneously detecting binding kinetics by simultaneously providing different concentration of a reagent in each channel, with the same binding agents in each channel, is a functional equivalent to detecting binding kinetics by increasing concentration of a reagent in the same channel over time. It is predictable that these two methods are functional equivalences because in each method, there are detections between one bound reagent, and another reagent, with different concentrations (from which kinetic data can be obtained, as is well understood in the art, and as disclosed by Ivarrson).

It is noted that Winkler et al. teach that screening will be performed by, for example, separating or cutting two halves of the device, enabling screening by, for

example, contacting with a fluorescein labeled antibody, or the like followed by photodetection. Column 12, lines 29-32. Thus the skilled artisan is suggested to utilize known photodetection techniques, such as that disclosed by Ivarrson, that provides the benefit of simultaneous analysis, such as kinetic analysis, of different sensor zones. Given the improvements of Ivarrson, the skilled artisan would have had reasonable expectation of success in providing such improvements to the Winkler et al. invention to allow for simultaneous analysis in the different sensor zones.

Applicant further claims simultaneously obtaining reference data from a plurality of interspots, each of the microspots located at a surface between at least two or more microspots (interpreted to mean that the reference data spots are between spots with the first and second binding member).

However Shah discloses an array for determining the relative amount of a biological molecule (e.g., a nucleic acid) a sample comprising a plurality of biological molecules immobilized to a plurality of discrete and known spots on a substrate surface to form an array of biological molecules, wherein the array of spots comprises a plurality of test spots (i.e., for binding, e.g., by hybridization, to molecules in a sample) and at least one calibration spot.. In one aspect, the calibration spot comprises an equimolar mixture of all the biological molecules spotted on the array. The array can further comprise at least a second calibration spot. In one aspect, additional calibration spots comprise an equimolar dilution of (or increase in) the mixture of biological molecules spotted on a first calibration spot. In one aspect, the array comprises a plurality of calibration spots. Each calibration spot can represent

a different equimolar dilution of the mixture of biological molecules spotted on the array. Control spots can provide a consistent result independent of the labeled sample bound, e.g., hybridized, to the array. The control spots can be used to generate a "normalization" or "calibration" curve to offset possible intensity errors between the two or more arrays. In one aspect of the methods of the invention, "calibration" curves are generated using arrays comprising a plurality of "control spots." The computer-implemented methods, computer program products and computer systems of the invention can calculate and display calibration/normalization curves from binding (e.g., hybridization) data read from control spots from two or more arrays. Column 8, line 42 to column9, line 10; see also column 20, lines 30-39.

It is predictable by one of ordinary skills in the art that providing controls in the interspots in a line between lines of analyte reaction spots in the Winkler device allows for consistent results [less error from background noise] , as well as generation of a calibration curve (as shown by Shah.)

Providing such a pattern with alternating multiple lines of analyte reaction spots and calibration spots meets the claimed limitation of a plurality of interspots located at a surface between at least two or more microspots. The skilled artisan would have recognized the benefits of convenience and efficiency of performing simultaneous reactions. The skilled artisan would have had reasonable expectation of success because both use of a control is well within the knowledge and skills of the ordinary artisan (and is also exemplified by Shah).

As to claim 30, SPR detection or Brewster angle reflectometry is disclosed by Ivarrson as discussed above (Ivarrson, column 9, liens 40-48.)

As to claims 31 and 43, the types of detection may be SPR as discussed above, and the parameter may be reflectance changes (Ivarrson, see for example, column 9, lines 1-9.)

As to claim 35, the deactivating step may be the washing step. As disclosed by Winkler et al, the substrate and the channel block are separated and, optionally, the entire substrate is washed with an appropriate material to remove any unwanted materials from the points where the channels contact the substrate. Column 9, lines 53-57.

As to claim 36, obtaining reference data from a region of the surface not included in a microspot (i.e., another microspot used for control purposes) is discussed above regarding Lambert.

As to claim 41, forming a second channel perpendicular to the first channel is discussed above by Winkler et al.

As to claims 42 and 46, a probe array is produced as discussed above regarding Winkler.

Claims 32, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler et al., 5,384,261, in view of Ivarsson, 6,493,097, and further in view of

Shah, 6,916,621, as applied to claim 29 above, and further in view of Natesan et al., 20020048792.

While Ivarsson teaches kinetic analysis in general as discussed above, there is no specific disclosure that the assay is to determine dissociation constant. Natesan et al. however teach in paragraph 0113 that a number of well-characterized assays are available for determining binding affinity, usually expressed as dissociation constant for DNA-binding proteins and the cognate DNA sequences to which they bind. While Ivarsson discloses only in general kinetic analysis, the skilled artisan would have the knowledge to analyze kinetic parameters such as dissociation constants as such is understood in the art, as shown by Natesan et al.

Claims 34 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler et al., 5,384,261, in view of Ivarsson, 6,493,097, and further in view of Shah, 6,916,621, as applied to claims 29 and 37 above, and further in view of Siddigi et al., 5,541,113.

While Ivarrson disclose a sensor surface such as gold or silver, for SPR detection technique (column 20, lines 40-45), Ivarrson is silent as to formation of the probes on the sensor. Thus, there is no disclosure of activating the surface by producing an electric field over the microspot.

Siddigi et al. however disclose that it is known that an electric field induces certain chemical reactions (col. 1, lines 51-56.) While the disclosure refers to a chemical reaction that can be detected, rather than for immobilizing a probe, the skilled

artisan would have recognized that an electric field would induce similar reactions in certain ligands that may be of interest in order to cause a reaction for immobilization purposes, and thus use of an electric field to induce binding in the invention of the combination of the teachings of Winkler et al. and Ivarsson would have been obvious.

Response

Applicants have submitted affidavits to swear behind the Lambert reference, which has now been withdrawn.

However providing interspots as a control would have been obvious to the skilled artisan because controls, and or calibration curves from the controls, to offset errors is well known in the art, and is also disclosed by Shah.

Applicant's remaining arguments are also not persuasive. Applicant assert that the conventional method to determine kinetic parameters uses the same first binding surface and thus serial dilution is dictated.

This is not persuasive because Winkler discloses using different concentrations of the target analyte through the different channels for simultaneous detection (paragraph 11, lines 17-35.) The combined teachings of Winkler and Ivarrson (which teaches kinetic analysis in general by increasing the concentration of one reagent) would suggest to the skilled artisan that the different concentrations of target analyte in the Winkler device can be used for kinetic analysis.

In other words, it is predictable by the skilled artisan that simultaneously detecting binding kinetics by simultaneously providing different concentration of a reagent in each channel, with the same binding agents in each channel, is a functional equivalent to detecting binding kinetics by increasing concentration of a reagent in the same channel over time. It is predictable that these two methods are functional equivalences because in each method, there are detections between one bound reagent, and another reagent, with different concentrations (from which kinetic data can be obtained, as is well understood in the art, and as disclosed by Ivarrson).

Applicant also argues that the disclosure by Ivarrson on "mass distribution kinetic data for, e.g., sample binding/desorption" is too general, and is more likely to refer to the conventional recurrent use of the same first binding member. However Examiner emphasizes that it is the combination of the teachings of Winkler and Ivarrson that suggests to the skilled artisan that the different concentrations of target analyte in the different channels as disclosed by Winkler device can be used for simultaneous kinetic analysis. Both Winkler and Ivarrson teach simultaneous analysis. Ivarrson teaches that assays with different concentrations of one of the binding reagents allow for obtaining binding kinetic data. Winkler teaches that different concentrations of one binding reagent can be provided in different channels.

As to Applicant's arguments that there would have been no expectation of success because there are known to be inefficiency and unpredictable new variables. This is not persuasive because the same inefficiencies and unpredictability exists with both types of assays (i.e., the "conventional" and the assay as recited by Applicant.)

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Thurs. 9-7:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641